UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,466	03/01/2002	Alexander Olek	81659A	6657

23685 7590 01/14/2008
KRIEGSMAN & KRIEGSMAN
30 TURNPIKE ROAD, SUITE 9
SOUTHBOROUGH, MA 01772

EXAMINER	
BRUSCA, JOHN S	
ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
01/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/087,466	OLEK ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14-18,20-23,25,26,30-34,36 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action contains a new grounds of rejection under 35 U.S.C. 101, and is therefore a non-final Office action.

Claim Objections

2. The objection to claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 in the Office action mailed 19 April 2007 is withdrawn in view of the amendment filed 22 October 2007. It is noted that the Office action mailed 19 April 2007 contained a typographical error in that cancelled claim 35 was listed instead of claim 36, as noted by the applicants in their response filed 22 October 2007.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-12, 14-18, 20-23, 25, 26, 30-34, and 36 are drawn to à process and claim 41 is drawn to a device that executes the process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). The instant claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998) below, the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result:

The question of whether a claim encompasses statutory subject matter should not focus on *which* of the four categories of subject matter a claim is directed to 9 -- process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Section 101 specifies that statutory subject matter must also satisfy the other "conditions and requirements" of Title 35, including novelty, nonobviousness, and adequacy of disclosure and notice. *See In re Warmerdam* , 33 F.3d 1354, 1359, 31 USPQ2d 1754, 1757-58 (Fed. Cir. 1994). For purpose of our analysis, as noted above, claim 1 is directed to a machine programmed with the Hub and Spoke software and admittedly produces a "useful, concrete, and tangible result." *Alappat* , 33 F.3d at 1544, 31 USPQ2d at 1557. This renders it statutory subject matter, even if the useful result is expressed in numbers, such as price, profit, percentage, cost, or loss.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful" the claim must produce a result that is specific and substantial. For a claim to be "concrete" the process must have a result that is reproducible. For a claim to be "tangible" the process must produce a real world result . Furthermore, the claim must be limited only to statutory embodiments.

Claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 do not require production of a tangible result in a form that is useful to the user of the process or apparatus. The claims conclude with addition of selected genes to a gene panel. A gene panel is discussed on pages 17-18 of the specification as a knowledge base present in forms of computer readable memory including a computer disc, RAM, and ROM, or a printed table. Data in the form of signals in

RAM and ROM or even a physical computer disc are not necessarily limited to tangible outputs that are in a format that is interpretable by a user of the claimed method or device. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment.

Claim Rejections - 35 USC § 112

4. The rejection of claims 1-12, 14-18, 20-23, 25, 26, 30-34, 35, and 41 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office action mailed 19 April 2007 is withdrawn in view of the amendment filed 22 October 2007.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of determining genes that have differences in expression and methylation relative to two cancerous biological samples. The specification

describes a method of determining genes that have differences in expression and methylation relative to two groups of samples on page 11, relative to healthy and/or diseases samples on page 12, and relative to prostate cancer cell lines and healthy prostate cells on page 21. The specification does not describe a method of determining genes that have differences in expression and methylation relative to two cancerous samples.

7. Claims 1-12, 14-18, 20-23, 25, 26, 30-34, 36, and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must make a gene paned useful for diagnostic and therapeutic purposes by comparison of the gene expression and DNA methylation levels of two cancerous samples. For the reasons discussed below there would be an unpredictable amount of experimentation required to make the claimed invention.

b) The specification presents guidance on pages 11 and 12 to compare healthy and diseased samples when practicing the claimed method.

c) The specification presents a working example on page 21 of comparison of prostate cancer cell line cells to healthy prostate cells when practicing the claimed invention.

d) The nature of the invention, molecular diagnostic assays, is complex.

e) Huang et al. shows a method of determining methylation sites relevant to breast cancer. Huang et al. shows in the abstract and throughout that the comparison was done between breast cancer cells and normal tissue so that differences that correlate with breast cancer could be determined.

f) The skill of those in the art of molecular diagnostic assays is high.

g) It is predictable from prior art such as Huang et la. that qualities of cancerous samples that are relevant to disease for diagnostic or therapeutic purposes should be compared to normal tissue controls so that the changes are known to appear only in diseases tissue.

h) The claims are broad in that they require determinations of gene panels useful for diagnostic or therapeutic purposes to be determined without determining whether the gene panels contain genes whose expression and methylation levels correlate with disease.

The skilled practitioner would first turn to the instant specification for guidance and working examples to practice the claimed method of making gene panels. However, the specification does not provide such guidance or working examples. Next, the skilled practitioner would turn to the prior art for such guidance. The prior art shows that genes related to disease

should be assessed relative to normal tissue controls. Finally, said practitioner would turn to trial and error experimentation to make and use the claimed subject matter, which represents undue experimentation.

Claim Rejections - 35 USC § 103

8. The rejection of claims 1-8, 10, 11, 14, 15, 17, 18, 20, 22, 23, 25, 26, 30-34, and 41 under 35 U.S.C. 103(a) as being unpatentable over Kikyo et al. as evidenced by New England Biolabs and Siegfried et al. in view of Frommer et al. in view of Huang et al. in the Office action mailed 19 April 2007 is withdrawn in view of the amendment filed 22 October 2007.

9. The rejection of claims 1, 6, 9, 16, 21, and 36 under 35 U.S.C. 103(a) as being unpatentable over Kikyo et al. as evidenced by New England Biolabs and Siegfried et al. in view of Frommer et al. in view of Huang et al. as applied to claims 1-8, 10, 11, 14, 15, 17, 18, 20, 22, 23, 25, 26, 30-34, and 41 above and further in view of Danssaert et al. in the Office action mailed 19 April 2007 is withdrawn in view of the amendment filed 22 October 2007.

10. The rejection of claims 1 and 12 under 35 U.S.C. 103(a) as being unpatentable over Kikyo et al. as evidenced by New England Biolabs and Siegfried et al. in view of Frommer et al. in view of Huang et al. as applied to claims 1-8, 10, 11, 14, 15, 17, 18, 20, 22, 23, 25, 26, 30-34, and 41 above, and further in view of Anderson et al. in the Office action mailed 19 April 2007 is withdrawn in view of the amendment filed 22 October 2007.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/John S. Brusca/
Primary Examiner
Art Unit 1631

jsb